IN THE CLAIMS

Amend the claims as indicated below by the markings. Cancel claims 3, 6, 8, 14, 15 and 16 without prejudice.

1. (Currently Amended) A transgenic mutant mouse ~~deficient in an endogenous Sigma-1 receptor~~, whose genome comprises a mutation comprising a disruption in a gene of an endogenous Sigma-1 receptor, wherein said gene disruption gives rise to a homozygous transgenic mutant mouse lacking detectable levels of endogenous Sigma-1 receptor, and wherein said transgenic mutant mouse is fertile and obtainable by the use of the vector identified as pHR53TK that is deposited in the CECT under access number CECT 5737, to insert a functional disruption in the endogenous Sigma-1 receptor.

Claims 2 - 4. (Cancelled)

5. (Previously Presented) The transgenic mutant mouse according to claim 1, wherein the genome of the transgenic mutant mouse comprises a transgene within the disrupted region introduced in the endogenous Sigma-1 receptor gene that comprises a sequence encoding a positive selection marker.

Claims 6 - 8. (Cancelled)

9. (Currently Amended) A homologous recombination vector with a positive-negative selection marker identified as pHR53TK, deposited in Spanish Type Culture Collection (CECT) of the University of Valencia with access number CECT 5737.

Claims 10 – 16. (Cancelled)

17. (Previously Presented) An isolated cell from a transgenic mouse, deficient in an endogenous Sigma-1 receptor, according to claim 1, or its offspring.

18. (Previously presented) The cell according to claim 17, comprising one or both mutated alleles of the Sigma-1 receptor gene.

19. (Previously presented) The cell according to claim 17, wherein the cell is propagated.

20. (Previously Presented) The offspring of a transgenic mutant mouse deficient in an endogenous Sigma-1 receptor, according to claim 1.

21. (Currently Amended) A process for making a mutant mouse ~~according to claim 1~~, comprising:

introducing a functional disruption in an endogenous Sigma-1 receptor gene present in a cell genome by homologous recombination in said cell between an allele of an endogenous Sigma-1 receptor gene and a homologous recombination vector with positive-negative selection according to claim 9,

selecting the recombinant homologues by the positive-negative selection technique,

introducing said recombinant homologues in embryos,

implanting said embryos receptor pseudogestating female mammals,

carrying, by the female mammals, the embryos to term,

selecting chimeras able to efficiently transmit the genotype of the recombinant homologues to their offspring by the germ line, and

crossing said chimeras with wild-type mice to obtain heterozygous mutants to disrupt the endogenous Sigma-1 receptor.

Claims 22 – 27. (Cancelled)

28. (Previously presented) The cell according to claim 19 wherein the cell is immortalized.

29. (Previously presented) The process according to claim 21, further comprising:

crossing said heterozygous mutants with each other to obtain homozygous mutants.

Claims 30, 31 and 32. (Cancelled)